

REC'D 27 JUN 2001

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference RTM	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP00/02887	International filing date (day/month/year) 28/03/2000	Priority date (day/month/year) 29/03/1999
International Patent Classification (IPC) or national classification and IPC G01N33/00		
Applicant ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 23/10/2000	Date of completion of this report 25.06.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer GONCALVES M L F C Telephone No. +49 89 2399 8127 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/02887

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-23 as originally filed

Claims, No.:

1-47,55-59 as originally filed

48-54 as received on 27/04/2001 with letter of 20/04/2001

Drawings, sheets:

1/12-12/12 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/02887

- ☐ the description, pages: 4, 5
- ☐ the claims, Nos.: 1-59
- ☐ the drawings, sheets: 1-59

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-46
	No:	Claims	1, 47-59
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-59
Industrial applicability (IA)	Yes:	Claims	1-59
	No:	Claims	

2. Citations and explanations
see separate sheet

Section V

1. Reference is made to the following documents:
D1: Proceedings TAS 96, Analytical Methods & Instrumentation, Special Issue μ TAS'96, 1996, pages 124-125.
D2: WO 98/49344
D3: US 5 585 069
D4: EP 0 649 534
2. The subject-matter of claim 1 is an apparatus comprising the following features: a) at least one reaction chamber; b) at least one fluid inflow channel communicating with the (or each) reaction chamber; and c) gate means adapted to prevent passage of aqueous fluid through the fluid inflow channel(s) into the reaction chamber(s) before a fluid entry force is applied; the gate means being characterised by at least the (or each) inflow channel having an hydrophobic inner surface.

D1 shows the detection of single DNA Molecules and DNA fragment analysis in moulded silicone elastomer microchips. An micro-channel device carrying a variety of channel layouts for specific applications and made out of the silicone elastomer polydimethylsiloxane (PDMS, an hydrophobic material) is described. The required buffer solutions and separation media are introduced in the channels by vacuum or by applying force of up to 1 bar (see page 124).

D2 relates to a method for analysing nucleic acids which comprises: (a) forming a micro channel structure in a substrate ; (b) treating at least a portion of the micro channel structure to produce a pattern of reactive, hydrophilic sites; (c) applying a different aqueous probe solution to each hydrophilic site to couple a number of probes to the micro channel structure, and (d) affixing a cover plate to the substrate to enclose the micro channel structure. Also claimed is an apparatus for carrying out the above mentioned method, wherein the surface of the micro channel structure is treated with an hydrophobic substance, thus forming an hydrophobic layer, and comprising means for electro kinetically or hydraulically transporting the fluid sample to the reactive probes sites (see claim 33 to 37).

From the above analysis of the prior art, the apparatus of claim 1 is not novel because the prior art devices already had the inflow channel(s) having an hydrophobic inner surface - the so called "gate means" in feature c) of claim 1- and

present the same advantages: introduction of the liquids achieved only by application of a fluid entry force. Hence, the subject-matter of claim 1 does not fulfil the requirements of Article 33(2) PCT.

3. The additional features introduced by the dependent claims 2-46 cannot be combined with the features of claim 1 to form a basis for inventive subject-matter, because the features introduced by these claims relate to details of construction that are either disclosed in the prior art documents cited in the search report or relate to standard options in the art (see D1 pages 124-125; D2 claims 33-68 and figures; D3 claims and figures, and D4 claims and figures).
4. The subject-matter of independent claim 47 (referring to a method of manufacturing the apparatus of the application) and of the claims 48-52 dependent thereon is also anticipated by the disclosures in document D1 (see pages 124 and 125) and in document D2 (see claims 1-20). Hence, the subject-matter of claims 47-52 does not fulfil the requirements of Article 33(2) PCT.
5. The subject-matter of independent claim 53 (referring to a method of operating the apparatus of the application) and of the claims 54-59 dependent thereon is also anticipated by the disclosures in the prior art documents D1 (see page 124) and D2 (see claims 66-68). Thus, the subject-matter of claims 53-59 does not fulfil the requirements of Article 33(2) PCT.
6. The newly filed claims 48-54 do not contravene the requirements of Article 34 (2) b) PCT.

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference RTM	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 00/ 02887	International filing date (day/month/year) 28/03/2000	(Earliest) Priority Date (day/month/year) 29/03/1999
Applicant ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (see Box II).

4. With regard to the title,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

MICROSCALE TOTAL ANALYSIS SYSTEM

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

☒ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

1

☐ None of the figures.

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Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
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CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

PC 00/02887

IPC 7 G01N33/00

B. FIELDS SEARCHED

IPC 7 GOIN

WPI Data

X	CARLO D. EFFENHAUSER, GERARD J. M. BRUIN, ARAN PAULUS AND MARKUS EHRAT: "Detection of Single DNA Molecules and DNA fragment Analysis in Moulded Silicone Elastomer Microchips" PROCEEDINGS TAS 96, ANALYTICAL METHODS & INSTRUMENTATION, SPECIAL ISSUE UTAS'96, 1996, pages 124-125, XP000916638 cited in the application page 124 -page 125	1-59
X	WO 98 49344 A (LOCKHEED MARTIN ENERGY RESEARC) 5 November 1998 (1998-11-05) claims 33-68	1-59
Y	EP 0 649 534 A (ABBOTT LAB) 26 April 1995 (1995-04-26) claims; figures	1-59

☒ Patent family members are listed in annex.

***&** document member of the same patent family

17/08/2000

GONCALVES M L F C

INTERNATIONAL SEARCH REPORT

International Application No

PC 00/02887

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 97 23773 A (SHIPMAN GREGORY K ; UNIVERSAL HEALTHWATCH INC (US); BERNSTEIN DAVID) 3 July 1997 (1997-07-03) claims; figures ----	1-59
A	TJERKSTRA R W ET AL: "ELECTROCHEMICAL FABRICATION OF MULTI WALLED MICRO CHANNELS" MICRO TOTAL ANALYSIS SYSTEMS. PROCEEDINGS OF THE UTAS WORKSHOP, 13 October 1998 (1998-10-13), pages 133-136-136, XP000874456 summary ----	1-59
A	US 5 017 473 A (WAGNER DANIEL B) 21 May 1991 (1991-05-21) cited in the application claims ----	1-59
A	US 4 621 059 A (ROKUGAWA KYUJI) 4 November 1986 (1986-11-04) cited in the application claims ----	1-59
A	US 5 624 850 A (KUMAR AMIT ET AL) 29 April 1997 (1997-04-29) cited in the application claims ----	
A	US 5 585 069 A (ZANZUCCHI PETER J ET AL) 17 December 1996 (1996-12-17) cited in the application claims -----	1-59

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/JP 00/02887

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9849344	A	05-11-1998	NONE	
EP 0649534	A	26-04-1995	US 5281540 A DE 69229801 D DE 69229801 T JP 7501149 T CA 2123785 A ES 2135419 T WO 9310454 A	25-01-1994 16-09-1999 09-03-2000 02-02-1995 23-05-1993 01-11-1999 27-05-1993
WO 9723773	A	03-07-1997	US 5766962 A AU 1294197 A	16-06-1998 17-07-1997
US 5017473	A	21-05-1991	NONE	
US 4621059	A	04-11-1986	JP 1970268 C JP 6105261 B JP 60186761 A DE 3583693 A EP 0156204 A	18-09-1995 21-12-1994 24-09-1985 12-09-1991 02-10-1985
US 5624850	A	29-04-1997	US 5976896 A	02-11-1999
US 5585069	A	17-12-1996	AU 705351 B AU 4152396 A AU 705659 B AU 4233796 A CA 2204912 A CA 2205066 A EP 0791238 A EP 0808456 A JP 11500602 T WO 9615450 A WO 9615576 A US 5681484 A US 5643738 A US 5593838 A US 5846396 A US 5985119 A US 5755942 A US 5863708 A US 5858804 A	20-05-1999 06-06-1996 27-05-1999 06-06-1996 23-05-1996 23-05-1996 27-08-1997 26-11-1997 19-01-1999 23-05-1996 23-05-1996 28-10-1997 01-07-1997 14-01-1997 08-12-1998 16-11-1999 26-05-1998 26-01-1999 12-01-1999

PCT REQUEST

RTM

Original (for SUBMISSION) - printed on 28.03.2000 11:07:44 AM

0	For receiving Office use only	
0-1	International Application No.	
0-2	International Filing Date	
0-3	Name of receiving Office and "PCT International Application"	
0-4	Form - PCT/RO/101 PCT Request	
0-4-1	Prepared using	PCT-EASY Version 2.90 (updated 08.03.2000)
0-5	Petition The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty	
0-6	Receiving Office (specified by the applicant)	European Patent Office (EPO) (RO/EP)
0-7	Applicant's or agent's file reference	RTM
I	Title of invention	CHEMICAL ASSAY APPARATUS
II	Applicant	
II-1	This person is:	applicant only
II-2	Applicant for	all designated States except US
II-4	Name	ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE
II-5	Address:	LABORATOIRE D'ELECTROCHIMIE DEPARTMENT DE CHIMIE-ICP III, CH-1015 LAUSANNE Switzerland
II-6	State of nationality	CH
II-7	State of residence	CH
III-1	Applicant and/or inventor	
III-1-1	This person is:	applicant and inventor
III-1-2	Applicant for	US only
III-1-4	Name (LAST, First)	ROSSIER, Joël S.
III-1-5	Address:	Ch. du Chamossaire 2, CH-1860 AIGLE Switzerland
III-1-6	State of nationality	CH
III-1-7	State of residence	CH

PCT REQUEST

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III-2	Applicant and/or inventor	
III-2-1	This person is:	applicant and inventor
III-2-2	Applicant for	US only
III-2-4	Name (LAST, First)	REYMOND, Frédéric
III-2-5	Address:	Ch. des Marionnettes 15, CH-1093 LA CONVERSION Switzerland
III-2-6	State of nationality	CH
III-2-7	State of residence	CH
III-3	Applicant and/or inventor	
III-3-1	This person is:	applicant and inventor
III-3-2	Applicant for	US only
III-3-4	Name (LAST, First)	GIRAULT, Hubert H.
III-3-5	Address:	CH-1088 ROPRAZ Switzerland
III-3-6	State of nationality	FR
III-3-7	State of residence	CH
IV-1	Agent or common representative; or address for correspondence The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:	agent
IV-1-1	Name (LAST, First)	MANATON, Ross Timothy
IV-1-2	Address:	J.Y. & G.W. Johnson, Kingsbourne House, 229-231 High Holborn, London, WC1V 7DP United Kingdom
IV-1-3	Telephone No.	+44 20 7405 0356
IV-1-4	Facsimile No.	+44 20 7831 9628
V	Designation of States	
V-1	Regional Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AP: GH GM KE LS MW SD SL SZ TZ UG ZW and any other State which is a Contracting State of the Harare Protocol and of the PCT EA: AM AZ BY KG KZ MD RU TJ TM and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT EP: AT BE CH&LI CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE and any other State which is a Contracting State of the European Patent Convention and of the PCT OA: BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG and any other State which is a member State of OAPI and a Contracting State of the PCT

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V-2	National Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AE AG AL AM AT AU AZ BA BB BG BR BY CA CH&LI CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW	
V-5	Precautionary Designation Statement In addition to the designations made under items V-1, V-2 and V-3, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except any designation(s) of the State(s) indicated under item V-6 below. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit.		
V-6	Exclusion(s) from precautionary designations	NONE	
VI-1	Priority claim of earlier national application		
VI-1-1	Filing date	29 March 1999 (29.03.1999)	
VI-1-2	Number	9907249.8	
VI-1-3	Country	GB	
VII-1	International Searching Authority Chosen	European Patent Office (EPO) (ISA/EP)	
VIII	Check list	number of sheets	electronic file(s) attached
VIII-1	Request	4	-
VIII-2	Description	23	-
VIII-3	Claims	8	-
VIII-4	Abstract	1	rtm-abstract.txt
VIII-5	Drawings	12	-
VIII-7	TOTAL	48	
VIII-8	Accompanying items	paper document(s) attached	electronic file(s) attached
VIII-8	Fee calculation sheet	✓	-
VIII-12	Priority document(s)	Item(s) VI-1	-
VIII-16	PCT-EASY diskette	-	diskette
VIII-18	Figure of the drawings which should accompany the abstract	1	
VIII-19	Language of filing of the international application	English,	
IX-1	Signature of applicant or agent		
IX-1-1	Name (LAST, First)	MANATON, Ross Timothy	

PCT REQUEST

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10-1	Date of actual receipt of the purported international application	
10-2	Drawings:	
10-2-1	Received	
10-2-2	Not received	
10-3	Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application	
10-4	Date of timely receipt of the required corrections under PCT Article 11(2)	
10-5	International Searching Authority	ISA/EP
10-6	Transmittal of search copy delayed until search fee is paid	

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11-1	Date of receipt of the record copy by the International Bureau	
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PCT (ANNEX - FEE CALCULATION SHEET)

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(This sheet is not part of and does not count as a sheet of the international application)

0	For receiving Office use only		
0-1	International Application No.		
0-2	Date stamp of the receiving Office		
0-4	Form - PCT/RO/101 (Annex)		
0-4-1	PCT Fee Calculation Sheet Prepared using	PCT-EASY Version 2.90 (updated 08.03.2000)	
0-9	Applicant's or agent's file reference	RTM	
2	Applicant	ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE, et al.	
12	Calculation of prescribed fees	fee amount/multiplier	total amounts (EUR)
12-1	Transmittal fee T	⇒	102
12-2	Search fee S	⇒	945
12-3	International fee		
	Basic fee (first 30 sheets) b1	409	
12-4	Remaining sheets	18	
12-5	Additional amount (X)	9	
12-6	Total additional amount b2	162	
12-7	b1 + b2 = B	571	
12-8	Designation fees		
	Number of designations contained in international application	85	
12-9	Number of designation fees payable (maximum 8)	8	
12-10	Amount of designation fee (X)	88	
12-11	Total designation fees D	704	
12-12	PCT-EASY fee reduction R	-126	
12-13	Total International fee (B+D-R) I	⇒	1,149
12-17	TOTAL FEES PAYABLE (T+S+I+P)	⇒	2,196
12-19	Mode of payment	authorization to charge deposit account	
12-20	Deposit account instructions The receiving Office:	European Patent Office (EPO) (RO/EP)	
12-20-1	is hereby authorized to charge the total fees indicated above to my deposit account	✓	
12-20-2	is hereby authorized to charge any deficiency or credit any over-payment in the total fees indicated above to my deposit account	✓	
12-21	Deposit account No.	28050017	
12-22	Date	28 March 2000 (28.03.2000)	

PCT (ANNEX - FEE CALCULATION SHEET)

RTM

Original (for SUBMISSION) - printed on 28.03.2000 11:07:44 AM

12-23	Name and signature	MANATON, Ross Timothy (for JY & GW JD #NJ&W) 
-------	--------------------	--

VALIDATION LOG AND REMARKS

13-2-3	Validation messages Names	Green? Applicant 1.:Telephone No. missing
		Green? Applicant 1.:Facsimile No. missing
		Green? Applicant 2.: Where several first/given names are indicated, they should preferably be separated by a comma. Please verify.
		Green? Applicant 4.: Where several first/given names are indicated, they should preferably be separated by a comma. Please verify.
		Yellow Applicant 4.:Street address missing
		Green? Agent 1.: Where several first/given names are indicated, they should preferably be separated by a comma. Please verify.
13-2-6	Validation messages Contents	Yellow! The power of attorney or a copy of the general power of attorney will need to be furnished unless all applicants sign the request form.
13-2-8	Validation messages Payment	Green? Please ensure that you have a valid deposit account with the receiving Office selected.

The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent, with the one chosen by the applicant. The file or two-letter code of that Authority may be indicated by the applicant on the line below:

IPEA/ EP

PCT

CHAPTER II

DEMAND

under Article 31 of the Patent Cooperation Treaty:

The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated).

For International Preliminary Examining Authority use only	
Identification of IPEA	Date of receipt of DEMAND
Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION	
Applicant's or agent's file reference RTM	
International application No. PCT/EP00/02887	International filing date (day/month/year) 28.03.00
(Earliest) Priority date (day/month/year) 29.03.99	
Title of invention MICROSCALE TOTAL ANALYSIS SYSTEM	
Box No. II APPLICANT(S)	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE Laboratoire d' Electrochimie, Department de Chimie-ICP III, CH-1015 Lausanne, SWITZERLAND.	
Telephone No.:	
Facsimile No.:	
Teleprinter No.:	
State (that is, country) of nationality: SWITZERLAND (CH)	State (that is, country) of residence: SWITZERLAND (CH)
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) ROSSIER, Joel S. Ch. du Chamossaire 2, CH-1860 AIGLE, SWITZERLAND.	
State (that is, country) of nationality: SWITZERLAND (CH)	State (that is, country) of residence: SWITZERLAND (CH)
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) REYMOND, Frédéric Ch. des Marionnettes 15, CH-1093 LA CONVERSION, SWITZERLAND.	
State (that is, country) of nationality: SWITZERLAND (CH)	State (that is, country) of residence: SWITZERLAND (CH)
<input checked="" type="checkbox"/> Further applicants are indicated on a continuation sheet.	

Continuation of Box No. II APPLICANT(S)

If none of the following sub-boxes is used, this sheet should not be included in the demand.

Name and address: (Family name followed by given name: for a legal entity: full official designation. The address must include postal code and name of country.)

GIRAULT, Herbert H.,
CH-1088 ROPRAZ,
SWITZERLAND.

State (that is, country) of nationality:
FRANCE (FR)

State (that is, country) of residence:
SWITZERLAND (CH)

Name and address: (Family name followed by given name: for a legal entity: full official designation. The address must include postal code and name of country.)

State (that is, country) of nationality:

State (that is, country) of residence:

Name and address: (Family name followed by given name: for a legal entity: full official designation. The address must include postal code and name of country.)

State (that is, country) of nationality:

State (that is, country) of residence:

Name and address: (Family name followed by given name: for a legal entity: full official designation. The address must include postal code and name of country.)

State (that is, country) of nationality:

State (that is, country) of residence:

☐

Further applicants are indicated on another continuation sheet.

Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The following person is ☒ agent ☐ common representative

and ☒ has been appointed earlier and represents the applicant(s) also for international preliminary examination.

☐ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.

☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

MANATON, ROSS TIMOTHY,
J.Y. & G.W. Johnson,
Kingsbourne House,
229-231 High Holborn,
London, WC1V 7DP,
UNITED KINGDOM.

Telephone No.:

+44 20 74050356

Facsimile No.:

+44 20 78319628

Teleprinter No.:

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION
Statement concerning amendments:*

1. The applicant wishes the international preliminary examination to start on the basis of:

☒ the international application as originally filed

the description ☐ as originally filed

☐ as amended under Article 34

the claims ☐ as originally filed

☐ as amended under Article 19 (together with any accompanying statement)

☐ as amended under Article 34

the drawings ☐ as originally filed

☐ as amended under Article 34

2. ☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.

3. ☐ The applicant wishes the start of the international preliminary examination to be postponed until the expiration of 20 months from the priority date unless the International Preliminary Examining Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). *(This check-box may be marked only where the time limit under Article 19 has not yet expired.)*

* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: ENGLISH
☒ which is the language in which the international application was filed.

☐ which is the language of a translation furnished for the purposes of international search.

☐ which is the language of publication of the international application.

☐ which is the language of the translation (to be) furnished for the purposes of international preliminary examination.

Box No. V ELECTION OF STATES

The applicant hereby elects all eligible States *(that is, all States which have been designated and which are bound by Chapter II of the PCT)*

excluding the following States which the applicant wishes not to elect:

Box No. VI CHECK LIST

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:

- | | | |
|--|---|--------|
| 1. translation of international application | : | sheets |
| 2. amendments under Article 34 | : | sheets |
| 3. copy (or, where required, translation) of amendments under Article 19 | : | sheets |
| 4. copy (or, where required, translation) of statement under Article 19 | : | sheets |
| 5. letter | : | sheets |
| 6. other (<i>specify</i>) | : | sheets |

For International Preliminary
Examining Authority use only

received not received

<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>

The demand is also accompanied by the item(s) marked below:

- | | |
|--|---|
| 1. <input checked="" type="checkbox"/> fee calculation sheet | 4. <input type="checkbox"/> statement explaining lack of signature |
| 2. <input type="checkbox"/> separate signed power of attorney | 5. <input type="checkbox"/> nucleotide and or amino acid sequence listing in computer readable form |
| 3. <input type="checkbox"/> copy of general power of attorney; reference number, if any: | 6. <input type="checkbox"/> other (<i>specify</i>): |

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).

MANATON, ROSS TIMOTHY (Agent)

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:

2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):

3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5. below, does not apply.

☐ The applicant has been informed accordingly.

4. ☐ The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5.

5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.

For International Bureau use only

Demand received from IPEA on:

PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Manaton, Ross Timothy
J.Y. & G.W. JOHNSON
Kingsbourne House
229-231 High Holborn
London WC1V 7DP
GRANDE BRETAGNE

PCT

WRITTEN OPINION

(PCT Rule 66)

Date of mailing (day/month/year)		20.11.2000
Applicant's or agent's file reference RTM		REPLY DUE within 3 month(s) from the above date of mailing
International application No. PCT/EP00/02887	International filing date (day/month/year) 28/03/2000	Priority date (day/month/year) 29/03/1999
International Patent Classification (IPC) or both national classification and IPC G01N33/00		
Applicant ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE		


- This written opinion is the **first** drawn up by this International Preliminary Examining Authority.
- This opinion contains indications relating to the following items:
 - I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain document cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application
- The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.
- The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 29/07/2001.

Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer / Examiner GONCALVES M L F C
	Formalities officer (incl. extension of time limits) Saavedra Martinez, V Telephone No. +49 89 2399 8621



I. Basis of the opinion

1. This opinion has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".*):

Description, pages:

1-23 as originally filed

Claims, No.:

1-59 as originally filed

Drawings, sheets:

1/12-12/12 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Claims 1, 47-59 (no)

Inventive step (IS) Claims 2-46 (no)

Industrial applicability (IA) Claims 1-59 (yes)

2. Citations and explanations
see separate sheet

Section V

1. Reference is made to the following documents:
D1: Proceedings TAS 96, Analytical Methods & Instrumentation, Special Issue μ TAS'96, 1996, pages 124-125.
D2: WO 98/49344
D3: US 5 585 069
D4: EP 0 649 534
2. The subject-matter of claim 1 is an apparatus comprising the following features: a) at least one reaction chamber; b) at least one fluid inflow channel communicating with the (or each) reaction chamber; and c) gate means adapted to prevent passage of aqueous fluid through the fluid inflow channel(s) into the reaction chamber(s) before a fluid entry force is applied; the gate means being characterised by at least the (or each) inflow channel having an hydrophobic inner surface.

D1 shows the detection of single DNA Molecules and DNA fragment analysis in moulded silicone elastomer microchips. An micro-channel device carrying a variety of channel layouts for specific applications and made out of the silicone elastomer polydimethylsiloxane (PDMS, an hydrophobic material) is described. The required buffer solutions and separation media are introduced in the channels by vacuum or by applying force of up to 1 bar (see page 124).

D2 relates to a method for analysing nucleic acids which comprises: (a) forming a micro channel structure in a substrate ; (b) treating at least a portion of the micro channel structure to produce a pattern of reactive, hydrophilic sites; (c) applying a different aqueous probe solution to each hydrophilic site to couple a number of probes to the micro channel structure, and (d) affixing a cover plate to the substrate to enclose the micro channel structure. Also claimed is an apparatus for carrying out the above mentioned method, wherein the surface of the micro channel structure is treated with an hydrophobic substance, thus forming an hydrophobic layer, and comprising means for electro kinetically or hydraulically transporting the fluid sample to the reactive probes sites (see claim 33 to 37).

From the above analysis of the prior art, the apparatus of claim 1 is not novel because the prior art devices already had the inflow channel(s) having an hydrophobic inner surface - the so called "gate means" in feature c) of claim 1- and

present the same advantages: introduction of the liquids achieved only by application of a fluid entry force. Hence, the subject-matter of claim 1 does not fulfil the requirements of Article 33(2) PCT.

3. The additional features introduced by the dependent claims 2-46 cannot be combined with the features of claim 1 to form a basis for inventive subject-matter, because the features introduced by these claims relate to details of construction that are either disclosed in the prior art documents cited in the search report or relate to standard options in the art (see D1 pages 124-125; D2 claims 33-68 and figures; D3 claims and figures, and D4 claims and figures).
4. The subject-matter of independent claim 47 (referring to a method of manufacturing the apparatus of the application) and of the claims 48-52 dependent thereon is also anticipated by the disclosures in document D1 (see pages 124 and 125) and in document D2 (see claims 1-20). Hence, the subject-matter of claims 47-52 does not fulfil the requirements of Article 33(2) PCT.
5. The subject-matter of independent claim 53 (referring to a method of operating the apparatus of the application) and of the claims 54-59 dependent thereon is also anticipated by the disclosures in the prior art documents D1 (see page 124) and D2 (see claims 66-68). Thus, the subject-matter of claims 53-59 does not fulfil the requirements of Article 33(2) PCT.

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Manaton, Ross Timothy
J.Y. & G.W. JOHNSON
Kingsbourne House
229-231 High Holborn
London WC1V 7DP
GRANDE BRETAGNE

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 71.1)

27 JUN 2001

Date of mailing
(day/month/year) 25.06.2001

Applicant's or agent's file reference
RTM

IMPORTANT NOTIFICATION

International application No.
PCT/EP00/02887

International filing date (day/month/year)
28/03/2000

Priority date (day/month/year)
29/03/1999

Applicant
ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

 European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Neumann, M

Tel. +49 89 2399-7351




PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference RTM	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP00/02887	International filing date (<i>day/month/year</i>) 28/03/2000	Priority date (<i>day/month/year</i>) 29/03/1999
International Patent Classification (IPC) or national classification and IPC G01N33/00		
Applicant ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 1 sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application 		
Date of submission of the demand 23/10/2000	Date of completion of this report 25.06.2001	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer GONCALVES M L F C Telephone No. +49 89 2399 8127	



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP00/02887

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-23 as originally filed

Claims, No.:

1-47,55-59 as originally filed

48-54 as received on 27/04/2001 with letter of 20/04/2001

Drawings, sheets:

1/12-12/12 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/02887

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-46
	No:	Claims	1, 47-59
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-59
Industrial applicability (IA)	Yes:	Claims	1-59
	No:	Claims	

2. Citations and explanations
see separate sheet

Section V

1. Reference is made to the following documents:

D1: Proceedings TAS 96, Analytical Methods & Instrumentation, Special Issue μ TAS'96, 1996, pages 124-125.

D2: WO 98/49344

D3: US 5 585 069

D4: EP 0 649 534

2. The subject-matter of claim 1 is an apparatus comprising the following features: a) at least one reaction chamber; b) at least one fluid inflow channel communicating with the (or each) reaction chamber; and c) gate means adapted to prevent passage of aqueous fluid through the fluid inflow channel(s) into the reaction chamber(s) before a fluid entry force is applied; the gate means being characterised by at least the (or each) inflow channel having an hydrophobic inner surface.

D1 shows the detection of single DNA Molecules and DNA fragment analysis in moulded silicone elastomer microchips. An micro-channel device carrying a variety of channel layouts for specific applications and made out of the silicone elastomer polydimethylsiloxane (PDMS, an hydrophobic material) is described. The required buffer solutions and separation media are introduced in the channels by vacuum or by applying force of up to 1 bar (see page 124).

D2 relates to a method for analysing nucleic acids which comprises: (a) forming a micro channel structure in a substrate ; (b) treating at least a portion of the micro channel structure to produce a pattern of reactive, hydrophilic sites; (c) applying a different aqueous probe solution to each hydrophilic site to couple a number of probes to the micro channel structure, and (d) affixing a cover plate to the substrate to enclose the micro channel structure. Also claimed is an apparatus for carrying out the above mentioned method, wherein the surface of the micro channel structure is treated with an hydrophobic substance, thus forming an hydrophobic layer, and comprising means for electro kinetically or hydraulically transporting the fluid sample to the reactive probes sites (see claim 33 to 37).

From the above analysis of the prior art, the apparatus of claim 1 is not novel because the prior art devices already had the inflow channel(s) having an hydrophobic inner surface - the so called "gate means" in feature c) of claim 1- and

present the same advantages: introduction of the liquids achieved only by application of a fluid entry force. Hence, the subject-matter of claim 1 does not fulfil the requirements of Article 33(2) PCT.

3. The additional features introduced by the dependent claims 2-46 cannot be combined with the features of claim 1 to form a basis for inventive subject-matter, because the features introduced by these claims relate to details of construction that are either disclosed in the prior art documents cited in the search report or relate to standard options in the art (see D1 pages 124-125; D2 claims 33-68 and figures; D3 claims and figures, and D4 claims and figures).
4. The subject-matter of independent claim 47 (referring to a method of manufacturing the apparatus of the application) and of the claims 48-52 dependent thereon is also anticipated by the disclosures in document D1 (see pages 124 and 125) and in document D2 (see claims 1-20). Hence, the subject-matter of claims 47-52 does not fulfil the requirements of Article 33(2) PCT.
5. The subject-matter of independent claim 53 (referring to a method of operating the apparatus of the application) and of the claims 54-59 dependent thereon is also anticipated by the disclosures in the prior art documents D1 (see page 124) and D2 (see claims 66-68). Thus, the subject-matter of claims 53-59 does not fulfil the requirements of Article 33(2) PCT.
6. The newly filed claims 48-54 do not contravene the requirements of Article 34 (2) b) PCT.

48. A method according to claim 47, wherein the apparatus is formed from polymeric material.

49. A method according to claim 48, wherein the apparatus is formed by injection moulding, hot embossing, photoablation, casting, or polymerisation on a mould.

50. A method according to claim 48 or claim 49, comprising the steps of forming a substrate having at least one depression therein, and applying an overlying layer over the substrate to seal the or each depression so as to form at least one fluid inflow channel and/or at least one reaction chamber.

51. A method according to claim 50, wherein the overlying layer is sealed with the substrate by thermal lamination.

52. A method according to claim 47, wherein at least a part of the apparatus is formed of a ceramics material, glass, a conductor or a semi-conductor material.

53. A method of operating an apparatus according to any of claims 1 to 46, comprising the steps of: placing at least one sample of an aqueous solution under test at the end of at least one fluid inflow channel distal at least one reaction chamber^{*}; causing the sample to enter the reaction chamber(s) via the fluid inflow channel(s) by applying a fluid entry force; and monitoring the sample in the reaction chamber(s) for the presence or concentration of a target substance.

54. A method according to claim 53, wherein the sample(s) is caused to exit the reaction chamber(s) before the reaction chamber(s) or the expelled sample is monitored for the presence or concentration of a target substance.

** , at least a portion of the or each fluid inflow channel having a hydrophobic inner surface*

TELECOPIER

European Patent Office,
D-80298 München,
GERMANY.

Attn: International Preliminary
Examining Authority

RTM/SMG

20th April 2001.

Dear Sirs,

International Patent Application PCT/EP00/02887
École Polytechnique Fédérale de Lausanne

I refer to the written opinion dated 20th November 2000 and to the communications regarding the extensions of the time limit in which to reply dated 26th February 2001 and 23rd March 2001.

I enclose herewith in triplicate replacement page 30 containing an amendment to Claim 53, and I ask that this page be substituted for the existing page of that number.

The amendment to Claim 53 is supported by the description at page 6 lines 30 to 32 and page 9 lines 1 to 2.

At item 2 of the written opinion the Examiner states that from an analysis of the prior art documents D1 and D2 "the apparatus of claim 1 is not novel because the prior art devices already had the inflow channel(s) having an hydrophobic inner surface - the so called "gate means" in feature c) of claim 1 (as identified by the Examiner) - and present the same advantages: introduction of the liquids achieved only by application of a fluid entry force. Hence, the subject-matter of claim 1 does not fulfil the requirements of Article 33(2) PCT".

D1 discloses a micro-channel device capable of carrying a variety of channel lay-outs for specific applications (see page 124 column, third paragraph), however D1 is solely concerned with the detection of single DNA molecules and DNA fragment analysis in moulded silicone elastomer microchips using fluorescent dyes. D1 does not suggest that the device described therein could be used to perform other chemical assays.

International Patent Application PCT/EP00/02887
École Polytechnique Fédérale de Lausanne

Furthermore, D1 does not disclose feature a) of Claim 1 of the present invention as identified by the Examiner i.e. at least one reaction chamber.

The device of D1 is made from polydimethylsiloxane (PDMS) (see page 124 column 2 second paragraph) which is a hydrophobic material. However, the authors of D1 do not state nor do they suggest that the hydrophobic properties of this material are important to the proper functioning of the device. It is also clear that all of the surfaces of the device of D1 are hydrophobic not just the fluid inflow channel as defined in the present application. In contrast only a portion of the device disclosed in the present application, namely the fluid inflow channel, is at least partially hydrophobic. The gating effect of the present invention is provided by the different surface hydrophobicities between the surface of the fluid inflow channel and the micro-channel network of the apparatus. The difference in hydrophobicity between the surface of the fluid inflow channel and the micro-channel network means that flow is possible before and/or after the gate. The gate of the present invention serves to stop the flow of aqueous solutions into the micro-channel network of the apparatus.

D1 does not disclose or suggest a fluid inflow channel providing gated access to a reaction chamber. Therefore Claim 1 of the present application is novel and inventive over D1.

With respect to D2 the Examiner states that D2 also claims an apparatus for carrying out a method "wherein the surface of the micro channel structure is treated with a hydrophobic substance, thus forming a hydrophobic layer, and comprising means for electro kinetically or hydraulically transporting the fluid sample to the reactive probe sites (see claim 33 to 37)".

In fact Claim 37 of D2 refers to the deposition of a hydrophobic layer on the surface of a microchannel structure at least a portion of which is removed to form a pattern of exposed sites. In this regard I would draw the Examiner's attention to page 8 lines 13-21 where it is stated that:

These spots may then be treated with a silane coupling agent as described above to produce reactive,

International Patent Application PCT/EP00/02887
École Polytechnique Fédérale de Lausanne

hydrophilic spots. An aqueous probe solution applied to an individual spot would be confined to its hydrophilic site and thus prevented from mixing with different probe solutions in adjacent spots. The intervening hydrophobic regions would also prevent probe mixing in the case of the other immobilization methods described above.

The hydrophobic regions disclosed in D2 are used to separate individual probes on the surface of the microchannel network. D2 does not disclose nor does it suggest a fluid inflow channel providing gated access to a reaction chamber.

Therefore Claim 1 of the present application is novel and inventive over D2.

With regard to item 3 of the written opinion it is submitted that Claim 1 is novel and inventive; therefore the novelty and inventiveness of any claims dependent thereon does not have to be examined.

In item 4 of the written opinion the Examiner considers that the subject-matter of independent Claim 47 and the claims dependent thereon is anticipated by the disclosures in document D1 and D2.

Neither D1 nor D2 disclose a method of manufacture of an apparatus having the feature "at least a portion of the or each fluid inflow channel having a hydrophobic inner surface adapted to act as gate means to prevent passage of fluid through the fluid inflow channel into the reaction chamber until such fluid is acted upon by a fluid entry force". Therefore, Claim 47 of the present application is novel and inventive over D1 and D2 for the reasons given in relation to Claim 1 above.

Similarly, at item 5 of the written opinion the Examiner states that the subject-matter of independent Claim 53 and of the claims dependent thereon is also anticipated by the disclosures in the prior art documents D1 and D2.

Claim 53 has been amended to include the feature "at least a portion of the or each fluid inflow channel having a hydrophobic inner surface".

20th April 2001.

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The addition of this feature distinguishes the subject matter of Claim 53 from either D1 or D2 for the reasons indicated above.

I look forward to receiving a more favourable International Preliminary Examination Report.

Yours faithfully,

ROSS T. MANATON

Encl.

48. A method according to claim 47, wherein the apparatus is formed from polymeric material.

49. A method according to claim 48, wherein the apparatus is formed by injection moulding, hot embossing, photoablation, casting, or polymerisation on a mould.

50. A method according to claim 48 or claim 49, comprising the steps of forming a substrate having at least one depression therein, and applying an overlying layer over the substrate to seal the or each depression so as to form at least one fluid inflow channel and/or at least one reaction chamber.

51. A method according to claim 50, wherein the overlying layer is sealed with the substrate by thermal lamination.

52. A method according to claim 47, wherein at least a part of the apparatus is formed of a ceramics material, glass, a conductor or a semi-conductor material.

53. A method of operating an apparatus according to any of claims 1 to 46, comprising the steps of: placing at least one sample of an aqueous solution under test at the end of at least one fluid inflow channel distal at least one reaction chamber^{*}; causing the sample to enter the reaction chamber(s) via the fluid inflow channel(s) by applying a fluid entry force; and monitoring the sample in the reaction chamber(s) for the presence or concentration of a target substance.

54. A method according to claim 53, wherein the sample(s) is caused to exit the reaction chamber(s) before the reaction chamber(s) or the expelled sample is monitored for the presence or concentration of a target substance.

* , at least a portion of the or each fluid inflow channel having a hydrophobic inner surface